UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,176	06/06/2005	Gary Lawrence French	IMA-031.01	1966

25181 7590 04/14/2010

FOLEY HOAG, LLP
PATENT GROUP, WORLD TRADE CENTER WEST
155 SEAPORT BLVD
BOSTON, MA 02110

EXAMINER	
BERTAGNA, ANGELA MARIE	
ART UNIT	**PAPER NUMBER**
1637	

MAIL DATE	DELIVERY MODE
04/14/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/914,176	FRENCH ET AL.	
	Examiner	Art Unit	
	Angela M. Bertagna	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-50,62-65 and 78-89* is/are pending in the application.

4a) Of the above claim(s) *45,47,80 and 82* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-44,46,48-50,62-65,78,79,81 and 83-89* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/24/2001*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Sequence Rules

1. Applicant's response filed on June 1, 2009 is acknowledged. The application now complies with 37 CFR 1.821-1.825.

Election/Restrictions

2. Applicant's election of SEQ ID NO: 4 in the reply filed on July 24, 2008 is acknowledged. The reply filed on July 24, 2008 does not state whether the election is made with traverse or without traverse. Since Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 45, 47, 80, and 82 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on July 24, 2008.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Priority

3. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

4. Applicant's submission of an Information Disclosure Statement on August 24, 2001 is acknowledged. A signed copy is enclosed.

Oath/Declaration

5. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective, because it does not state that the person making the oath or declaration acknowledges the duty to disclose to the Office all information known to the person to be "material to patentability as defined in 37 CFR 1.56."

Drawings

6. The drawings filed on August 24, 2001 are acceptable.

Specification

7. The disclosure is objected to because of the following informalities:

(A) The specification does not contain section headings to identify the different portions of the disclosure.

(B) The specification contains sequences on pages 4 and 12 that are not identified by the appropriate sequence identifier as required by 37 CFR 1.821.

(C) The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: The specification fails to provide proper antecedent basis for detection of *Proteus spp.*, *Enterobacter spp.*, *Enterococcus spp.*, *Klebsiella spp.*, and *Pneumococci* as recited in claim 41, because these organisms are only mentioned in the original claims and the abstract. It is also noted that the specification does not provide proper antecedent basis for kits, in general, because they are only mentioned in the abstract and original claims. As discussed in greater detail below, the kits of claims 62-65, 62-65, 78, 79, 81, 83-85, and 89 have been rejected for introducing new matter. Should Applicant overcome the new matter rejection, the issue of proper antecedent basis in the specification for kits would need to be addressed.

(D) The Article 34 amendment present in the specification is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The replacement pages, pages 4 and 4A, contain material at page 4, lines 22-31 and page 4A, lines 5-7 that does not appear in, and therefore, is not supported by the original disclosure. As noted in MPEP 1893.01(b), "The fact that an amendment made to the international application during the international phase was entered in the national stage

application does not necessarily mean that the amendment is proper. Specifically, amendments are not permitted to introduce 'new matter' into the application. See PCT Article 34(2)(b). Where it is determined that such amendments introduce new matter into the application, then the examiner should proceed as in the case of regular U.S. national applications filed under 35 U.S.C. 111(a) by requiring removal of the new matter and making any necessary rejections to the claims. See MPEP § 608.04 and § 2163.06." Applicant is required to cancel the new matter in the reply to this Office Action.

Appropriate correction is required.

Claim Interpretation

8. Prior to analysis of the art, the claims must be construed. As noted in MPEP 2111, citing *Phillips v. AWH Corp.*, 415 F.3d 1303, 75 USPQ2d 1321 (Fed. Cir. 2005), "During patent examination, the pending claims must be 'given their broadest reasonable interpretation consistent with the specification.'

The instant claims are drawn to methods and kits comprising an oligonucleotide primer comprising **a** sequence as shown in SEQ ID NO: 1, an oligonucleotide primer comprising **a** sequence as shown in SEQ ID NO: 2, and an oligonucleotide probe having **a** sequence as set forth in SEQ ID NO: 4. The broadest reasonable interpretation of the language "a sequence" encompasses any portion (*i.e.* a dinucleotide or larger) of the claimed sequences. This interpretation is reflected in the discussion below.

Claim Rejections - 35 USC § 112, 1st paragraph (New Matter)

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 39-44, 46, 48-50, 62-65, 78, 79, 81, and 83-89 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

As noted in *In re Wright*, 866 F.2d 422, 9USPQ2d 1649 (Fed. Cir. 1989), "An amendment to the claims or the addition of a new claim must be supported by the description of the invention in the application as filed." Also, as noted in *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981), "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement."

Claims 39-44, 46, and 48-50 are drawn to methods for identifying bacteria in a test sample that comprise amplification with universal primers that target the 23S rRNA gene and *comprise a sequence* as shown in SEQ ID NO: 1 and *a sequence* as shown in SEQ ID NO: 2 followed by hybridization with oligonucleotide probes. Claims 62-65, 78, 79, 81, 83-85, and 89 are drawn to kits comprising a primer *having a sequence* as shown in SEQ ID NO: 1, a primer *having a sequence* as shown in SEQ ID NO: 2, and one or more oligonucleotide probes capable of hybridizing to an amplification product produced using SEQ ID NO: 1 and SEQ ID NO: 2 as primers. Claims 86-88 are drawn to primer pair comprising a first primer *comprising a sequence* as shown in SEQ ID NO: 1 and *a*

sequence as shown in SEQ ID NO: 2. The claimed genus of oligonucleotide primers includes oligonucleotides consisting of SEQ ID NO: 1 or SEQ ID NO: 2, oligonucleotides consisting essentially of SEQ ID NO: 1 and SEQ ID NO: 2, oligonucleotides comprising SEQ ID NO: 1 and SEQ ID NO: 2, and oligonucleotides comprising a sequence (*i.e.*, a portion) of SEQ ID NO: 1 and SEQ ID NO: 2.

Applicant has stated that the amendments to the claims are supported at least by the original claims in the international application and the Article 34 amendment filed on March 5, 2001 (see page 7 of the response filed on August 24, 2001).

The original disclosure, including the original claims, has been reviewed, but proper support does not exist for the full scope of the methods and products recited in the instant claims. The original disclosure provides support for oligonucleotide primers consisting of or consisting essentially of SEQ ID NO: 1 and SEQ ID NO: 2 (see the abstract, pages 3-4, and original claims 1, 13, and 14), but it does not provide support for the broader oligonucleotide primer recitations contained in the instant claims, because there is no discussion of primers as more broadly defined in the instant claims.

The original disclosure also does not provide adequate support for the kits recited in claims 62-65, 78, 79, 81, 83-85, and 89, because only kits comprising primers **or** probes are taught in the original disclosure (see abstract and original claims 25-27), whereas the claimed kits comprise both primers **and** probes in a single kit. Claims 25 and 26 of the Article 34 amendment are drawn to kits comprising oligonucleotide primers and probes. However, it is noted that Article 34 amendments are not part of the original disclosure, and therefore, cannot be relied upon to provide support under 35 U.S.C. 112, first paragraph for the claimed subject matter. As noted in MPEP 1893.01(b), "The fact

that an amendment made to the international application during the international phase was entered in the national stage application does not necessarily mean that the amendment is proper. Specifically, amendments are not permitted to introduce 'new matter' into the application. See PCT Article 34(2)(b). Where it is determined that such amendments introduce new matter into the application, then the examiner should proceed as in the case of regular U.S. national applications filed under 35 U.S.C. 111(a) by requiring removal of the new matter and making any necessary rejections to the claims. See MPEP § 608.04 and § 2163.06."

Accordingly, claims 39-44, 46, 48-50, 62-65, 78, 79, 81, and 83-89 have been rejected under 35 U.S.C. 112, first paragraph for incorporating new matter.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 39-44, 46, 48, 49, 62, 64, 65, 78, 79, 81, and 83-89 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bergeron et al. (US 5,994,066) in view of Gurtler et al. (Microbiology (1996) 142: 3-16) and further in view of Brosius et al. (Proceedings of the National Academy of Sciences, USA (1980) 18(7): 201-204) and further in view of Lowe et al. (Nucleic Acids Research (1990) 18(7): 1757-1761).

Claims 39-44, 46, 48, and 49 are drawn to methods for identifying bacteria in a test sample that comprise amplification with universal primers that target the 23S rRNA gene and have a sequence as shown in SEQ ID NO: 1 and a sequence as shown in SEQ ID NO: 2 followed by hybridization with oligonucleotide probes. Claims 62, 64, 65, 78, 79, 81, 83-85, and 89 are drawn to kits comprising a primer having a sequence as shown in SEQ ID NO: 1, a primer having a sequence as shown in SEQ ID NO: 2, and one or more oligonucleotide probes capable of hybridizing to an amplification product produced using SEQ ID NO: 1 and SEQ ID NO: 2 as primers. Claims 86-88 are drawn to primer pair comprising a first primer comprising a sequence as shown in SEQ ID NO: 1 and a sequence as shown in SEQ ID NO: 2.

Bergeron teaches methods, kits, and primer pairs for identifying bacteria present in a test sample (see abstract and column 3, line 60 – column 4, line 65).

Regarding claims 39-43, 44, 46, and 86, Bergeron teaches a method for identifying bacteria present in a test sample that comprises amplifying 23S rDNA in the test sample using a pair of universal primers that target conserved regions of the 23S

rRNA and detecting the amplification products using a plurality of sequence-specific oligonucleotide probes (see, for example, the abstract, column 3, line 60 – column 4, line 38, column 5, line 54 – column 6, line 35, column 12, lines 4-56, column 15, lines 1-55, and Annex III at columns 47-50). Bergeron teaches that the method may be used to simultaneously identify at least ten bacterial species in a test sample, including *Escherichia coli*, *Klebsiella pneumoniae*, *Enterococcus feacalis*, *Staphylococcus aureus*, *Enterococcus faecum*, *Proteus mirabilis*, and *Pseudomonas aeruginosa* (see abstract, column 3, line 60 – column 4, line 55, and columns 21-22, for example).

Regarding claims 48 and 49, Bergeron teaches that the amplification step may be PCR or transcription-mediated amplification (see, for example, column 4, line 66 – column 5, line 5 and column 21, lines 5-20).

Regarding claims 62, 78, 79, 81, and 83-85, and 89, Bergeron teaches kits that comprise the disclosed universal oligonucleotide primers and sequence-specific oligonucleotide probes (see column 4, lines 39-65 and columns 21-22, for example).

Regarding claims 64, 65, 87, and 88, Bergeron teaches that at least one of the universal primers may be labeled with a fluorophore or any other detectable label (column 20, line 55-67). Bergeron also teaches that nucleic acids may be labeled with a digoxigenin label (column 11, lines 15-29).

As noted above, Bergeron expressly teaches designing universal amplification primers from the gene encoding the 23S rRNA. However, Bergeron does not teach the use of primers comprising SEQ ID NO: 1 and SEQ ID NO: 2 or an oligonucleotide probe having a sequence as shown in SEQ ID NO: 4. Also, as noted above, Bergeron teaches that at least one of the primers used in the amplification method may be labeled with a

fluorophore or any other label and further discloses the use of digoxigenin as a suitable label for oligonucleotide probes, but the reference does not explicitly teach labeling at least one of the universal primers with digoxigenin as required by the instant claims.

Gurtler teaches a method for identifying bacteria in a test sample that comprises amplifying the 16S-23S spacer region using a first primer that targets a conserved region of the 16S rRNA gene and a second primer that targets a conserved region of the 23S rRNA gene, thereby generating a plurality of amplification products corresponding to the bacterial species present in the test sample, and identifying the different amplification products (see pages 8-9 and 13). Gurtler teaches that conserved regions of the 23S rRNA gene include those regions targeted by primers of the instant SEQ ID NO: 1 and SEQ ID NO: 2 (see Table 1 on page 5, where regions 6, 9, and 10 are described).

Brosius teaches the nucleic acid sequence of the 23S rRNA gene from *E. coli* (see abstract and Figure 2). The instant SEQ ID NO: 2 is contained in the sequence shown in Figure 2 of Brosius. Also, a sequence as shown in SEQ ID NO: 1 and SEQ ID NO: 4 are contained in Figure 2 of Brosius.

Lowe teaches a computer program for designing all possible oligonucleotide primers from a known nucleic acid sequence based on a set of user-specified conditions (see abstract and pages 1757-1758). Lowe teaches that the disclosed program simplifies and automates oligonucleotide primer design (see pages 1757-1758 and pages 1760-1761).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to practice the methods of Bergeron using a primer having a sequence as shown in SEQ ID NO: 1, a primer having a sequence as shown in SEQ ID NO: 2, and

an oligonucleotide probe having a sequence as shown in SEQ ID NO: 4. It also would have been *prima facie* obvious for the ordinary artisan to include the aforementioned primers and probe in the kits disclosed by Bergeron. As noted above, Bergeron expressly taught practicing the disclosed methods using universal primers targeting the 23S rRNA gene and a plurality of sequence-specific oligonucleotide probes. In conducting this embodiment of the methods disclosed by Bergeron, the ordinary artisan would have been motivated to design the universal oligonucleotide primers suggested by Bergeron from regions of the 23S rRNA gene known to be conserved among bacteria, such as the regions identified by Gurtler in Table 1, recognizing their suitability for the intended purpose. Doing so would result in the design of a primer having a sequence as shown in SEQ ID NO: 1, a primer having a sequence as shown in SEQ ID NO: 2, and a probe having a sequence as shown in SEQ ID NO: 4. Since, as evidenced by Brosius, the complete 23S rRNA gene sequence was known in the art at the time of the invention, and since methods for designing oligonucleotide primers and probes were also well-known in the art at the time of the invention, as evidenced by Lowe, the ordinary artisan would have had a reasonable expectation of success in making and using universal primers and sequence-specific probes targeting the 23S rRNA gene, such as the claimed primers and probe, as suggested by Bergeron.

Attention is also directed to *KSR Int'l Co. v. Teleflex Inc.* (550 U.S.____, 127 S. Ct. 1727 (2007)) where the Supreme Court determined that "a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try

might show that it was obvious under § 103 (*KSR*, 550 U.S. at ____, 82 USPQ2d at 1397)."

In this case, the prior art of Gurtler identified conserved regions of the gene encoding the 23S rRNA and further taught that universal oligonucleotide primers could be designed from these conserved regions (see above). These teachings in the prior art would have suggested to the ordinary artisan a finite number of possible universal oligonucleotide primers that could be designed from the 23S rRNA gene. An ordinary artisan would have expected predictable results, and thus would have had a reasonable expectation of success, in pursuing this finite number of possible oligonucleotides suggested by the prior art of Gurtler, since, as evidenced by Lowe, methods for designing and synthesizing oligonucleotide primers and probes were well-known in the art at the time of invention, and since, as evidenced by Brosius, the complete 23S rRNA gene sequence from *E. coli* was known in the art at the time of the invention.

Finally, regarding claims 64, 65, 87, and 88, it would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to label at least one of the primers resulting from the combined teachings of Bergeron, Gurtler, Brosius, and Lowe using any label known to be suitable for labeling oligonucleotides, such as the digoxigenin label taught by Bergeron, recognizing its suitability for the intended purpose. As noted in MPEP 2144.07, it is *prima facie* obvious to select a known material based on its suitability for the intended purpose in the absence of unexpected results. In this case, the teachings of Bergeron cited above would have indicated to the ordinary artisan that digoxigenin was a suitable molecule for labeling oligonucleotide primers, and therefore, the ordinary artisan would have been motivated to select this known material with a

reasonable expectation of success based on its suitability for the intended purpose. It is also noted that no evidence of unexpected results with respect to the use of digoxigenin labels has been presented. Thus, the methods of claims 39-44, 46, 48, and 49, the kits of claims 62, 64, 65, 78, 79, 81, 83-85, and 89, and the primer pairs of claims 86-88 are *prima facie* obvious in view of the combined teachings of the cited references.

13. Claims 50 and 63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bergeron et al. (US 5,994,066) in view of Gurtler et al. (Microbiology (1996) 142: 3-16) and further in view of Brosius et al. (Proceedings of the National Academy of Sciences, USA (1980) 18(7): 201-204) and further in view of Lowe et al. (Nucleic Acids Research (1990) 18(7): 1757-1761) and further in view of Kawasaki et al. (Methods in Enzymology (1993) 218: 369-381).

Claims 50 and 63 are drawn to the method of claim 39 and the kit of claim 62, respectively, wherein the oligonucleotides are attached to a support material.

As discussed above, the combined teachings of Bergeron, Gurtler, Brosius, and Lowe render obvious the methods of claims 39-44, 46, 48, and 49, the kits of claims 62, 64, 65, 78, 79, 81, 83-85, and 89, and the primer pairs of claims 86-88.

The combined teachings of Bergeron, Gurtler, Brosius, and Lowe do not suggest immobilizing the oligonucleotide probes on a solid support material as required by claims 50 and 63.

Kawasaki teaches a method, termed "reverse dot blot hybridization" that comprises performing DNA amplification and hybridizing the amplified products to an array of support-immobilized oligonucleotide probes that are specific to particular

amplification products (see page 370, Figure 1, and page 372). Kawasaki teaches that "It is the ability of PCR to amplify the target DNA sequences to high concentration that has allowed us to 'reverse' the conventional dot-blot approach (immobilized target DNA and labeled oligonucleotide probes in solution at high concentration) and use a labeled target DNA sequence (present after amplification at high concentration) in solution to hybridize with a panel of immobilized oligonucleotide probes (page 370)." Kawasaki further teaches that the disclosed reverse dot blot method is "a simple and rapid diagnostic procedure that allows screening of sample for a variety of mutations/polymorphisms in a single hybridization reaction (page 380)."

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of the invention to immobilize the sequence-specific oligonucleotide probes used in the methods and kits suggested by the combined teachings of Bergeron, Gurtler, Brosius, and Lowe on a solid support. Since Kawasaki taught that the disclosed reverse dot blot hybridization method was simpler and more rapid compared to methods in which amplified nucleic acids are immobilized on a solid support and probed with solution-phase oligonucleotides (*i.e.*, the methods disclosed by Bergeron), because only a single support is required for reverse dot blot hybridization (see pages 371-372 of Kawasaki), the ordinary artisan would have been motivated to immobilize the sequence-specific oligonucleotides on a solid support instead of the amplified target nucleic acids when practicing the methods and forming the kits suggested by the combined teachings of Bergeron, Gurtler, Brosius, and Lowe. Since the methods suggested by the combined teachings of Bergeron, Gurtler, Brosius, and Lowe were conducted using nucleic acid amplification products, an ordinary artisan would have had a reasonable expectation of

success in using immobilized oligonucleotide probes instead of immobilized amplified nucleic acids based on the teachings of Kawasaki at page 370. Also, since Kawasaki taught methods for immobilizing a plurality of oligonucleotides on a solid support (see pages 372-375), an ordinary artisan would have had a reasonable expectation of success in obtaining and using immobilized sequence-specific oligonucleotides when practicing the methods and forming the kits suggested by the combined teachings of Bergeron, Gurtler, Brosius, and Lowe. Thus, the method of claim 50 and the kit of claim 63 are *prima facie* obvious in view of the combined teachings of the cited references.

Conclusion

14. No claims are currently allowable.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Mabilat et al. (WO 96/24686 A2; cited on the IDS) teaches a primer that is similar to the instant SEQ ID NO: 1 (see page 14). Van Camp et al. (Current Microbiology (1993) 27: 147-151) teach methods for making and using universal primers targeting the 23S rRNA gene (see abstract and page 147). McCabe et al. (Molecular Genetics and Metabolism (1999) 66: 205-211) teach a method for identifying bacterial species present in a sample that comprises DNA amplification using universal primers targeting the 16S rRNA gene followed by hybridization with species-specific oligonucleotide probes (see abstract and pages 206-208).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Angela M. Bertagna whose telephone number is (571)272-8291. The examiner can normally be reached on M-F, 9- 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Angela M Bertagna/
Examiner, Art Unit 1637